Nrf2 Activator™

Antioxidant & Detoxification Support Formula*

Available in 30 capsules & 60 capsules

Clinical Applications

- Antioxidant Support*
- Attenuates the Expression and Release of Damaging Cytokines, Such as NF-κB*
- Supports the Body's Natural Detoxification Pathways*

***Nrf2 Activator™**, developed by Dr. David Perlmutter, is an exclusive formula designed to activate the Nrf2 genetic pathway. This pathway regulates the production of important molecules that impart antioxidant activity, such as glutathione and superoxide dismutase (SOD). It also regulates the production of detoxification enzymes, including glutathione S-transferase, and downregulates signaling factors such as NF-κB. Each ingredient in this formula is backed by extensive research in peer-reviewed journals.**

Discussion

Nrf2 (NF-E2-related factor 2), a transcription factor in humans that is encoded by the NFE2L2 gene, regulates the expression of a set of antioxidant and detoxifying genes, protecting the body from the ravages of oxidative stress-related conditions, including (but not limited to) those affecting the brain and nervous system. In an unstressed state, Nrf2 is anchored in the cytoplasm by its specific inhibitor Keap1 (kelch-like ECH-associated protein 1). Keap1 functions as a sensor for oxidants and electrophilic xenobiotics. In the presence of any of these substances, Keap1 gives up its inhibition of Nrf2. This action stabilizes Nrf2, allowing it to accumulate in the nucleus and bind to the antioxidant response element (ARE) located in the enhancers of its target genes. Under this circumstance, Nrf2 then upregulates a variety of antioxidant enzymes and detoxifying proteins.*

A variety of natural substances have been shown to activate Nrf2:

Sulforaphane (SGS), a naturally occurring isothiocyanate derived from cruciferous vegetables, induces phase 2 cytoprotective enzymes, supporting the body's response to cellular insult. SGS may modify critical cysteine residues of Keap1, leading to Nrf2 stabilization and activation of the ARE and thereby inducing phase 2 enzymes. Research demonstrates that sulforaphane, through induction of Nrf2-dependent phase 2 enzymes, protects the brain against hypoxic-ischemic injury and may improve cognitive function when administered following traumatic brain injury.*

Pterostilbene, a naturally occurring phenolic compound/analog of resveratrol that has comparatively better oral bioavailability, has been shown to possess cytotoxic, cytokine-inhibiting, and antioxidant properties. Resveratrol has also been shown to increase the protein and mRNA expression of Nrf2. There is evidence that Nrf2-mediated attenuation of oxidative stress and cytokine induction could be partially responsible for resveratrol's potential effect on cell-life regulation. In rat and animal studies, resveratrol/pterostilbene have been shown to upregulate a significant number of genes involved in mitochondrial function as well as to modulate cholinergic neurotransmission and improve cognition.*

Curcumin's array of biological activities stems from its cytokine-balancing activity, antioxidant properties, and induction of phase 2 detoxifying enzymes such as heme oxygenase-1 (HO-1). Purification of curcumin yields the curcuminoids demethoxy curcumin (DMC) and bisdemethoxy curcumin (BDMC). DMC has been shown to induce HO-1 more effectively than curcumin. The ability of DMC and BDMC to induce the expression of HO-1 and to translocate Nrf2 to the nucleus of pancreatic beta cells in mice suggests that they may play a role in cellular defense. Human studies showed a significant increase in curcumin absorption when co-administered with BioPerine®, a patented black pepper extract.*

Green Tea's major polyphenol, (-)-epigallocatechin-3-gallate (EGCG), has been shown to induce expression of glutathione S-transferase, glutathione peroxidase, glutamate cysteine ligase, HO-1, and other enzymes, thereby protecting a variety of cells, including cultured neurons, against oxidative stress-induced cell death. EGCG modulates the redox-sensitive transcription factor Nrf2, which plays a key role in activating detoxifying enzyme HO-1 as well as other phase 2 enzymes.*

In summary, Nrf2 Activator is a promising approach to increasing antioxidant defenses by transcriptionally increasing the activity of the Nrf2/ARE pathway and positively affecting the transcription of damaging cytokine and antioxidant genes. Green tea, curcumin, and resveratrol (pterostilbene) have also been shown to influence amyloid formation; this influence further increases the potential of this innovative formula.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Nrf2 Activator™ Supplement Facts

Serving Size: 2 Capsules

	Amount Per Serving	%DV
Glucoraphanin (from broccoli extract)(*Brassica oleracea italica*)(seed) (SGS™)	60 mg	**
Turmeric Extract (*Curcuma longa*)(rhizome)(95% curcuminoids)	400 mg	**
Green Tea Aqueous Extract (*Camellia sinensis*)(leaf)(80% polyphenols, 60% catechins, 30% EGCG, 6% caffeine)	400 mg	**
trans-Pterostilbene (pTeroPure®)	100 mg	**
Black Pepper Extract (*Piper nigrum*)(fruit)(BioPerine®)	4 mg	**

** Daily Value (DV) not established.

Other Ingredients: HPMC (capsule), stearic acid, magnesium stearate, silica, and medium-chain triglycerides.
BioPerine is a registered trademark of Sabinsa Corp. BioPerine is protected by US patents 5,536,506; 5,744,161; 5,972,382; and 6,054,585.
pTeroPure is a trademark of ChromaDex, Inc.

DIRECTIONS: Take one to two capsules daily, or as directed by your healthcare practitioner.

Children, pregnant and lactating women, and individuals using blood thinners or receiving cancer treatment should consult their healthcare practitioner prior to use. Do not use if tamper seal is damaged.

DOES NOT CONTAIN: Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs) artificial colors, artificial sweeteners, or preservatives.

STORAGE: Keep tightly closed in a cool, dry place out of reach of children.

Produced under US patents 5,725,895; 5,968,505; 5,968,567; 6,177,122 and 6,242,018 licensed from Brassica Protection Products LLC; SGS is a trademark of Brassica Protection Products LLC.

VEGETABLE CAPSULES

References

1. Kim J, et al. Naturally occurring phytochemicals for the prevention of Alzheimer's disease. *J Neurochem*. 2010 Mar;112(6):1415-30 [PMID: 20050972]
2. Ping Z, et al. Sulforaphane protects brains against hypoxic-ischemic injury through induction of Nrf2-dependent phase 2 enzyme. *Brain Res*. 2010 Apr 24. [PMID: 20417626]
3. Dash PK, et al. Sulforaphane improves cognitive function administered following traumatic brain injury. *Neurosci Lett*. 2009 Aug 28;460(2):103-7 [PMID: 19515491]
4. Ahn YH. Electrophilic tuning of the chemoprotective natural product sulforaphane. *Proc Natl Acad Sci U S A*. 2010 May 25;107(21):9590-5. [PMID: 20439747]
5. Beal MF. Therapeutic approaches to mitochondrial dysfunction in Parkinson's disease. *Parkinsonism Relat Disord*. 2009 Dec;15 Suppl 3:S189-94 [PMID: 20082988]
6. Bishayee A, et al. Resveratrol suppresses oxidative stress and inflammatory response in diethylnitrosamine-initiated rat hepatocarcinogenesis. *Cancer Prev Res (Phila Pa)*. 2010 Jun;3(6):753-63. Epub 2010 May 25. [PMID: 20501860]
7. Schmatz R, et al. Resveratrol prevents memory deficits and the increase in acetylcholinesterase activity in streptozotocin-induced diabetic rats. *Eur J Pharmacol*. 2009 May 21;610(1-3):42-8 [PMID: 19303406]
8. Yang C, et al. Curcumin upregulates transcription factor Nrf2, HO-1 expression and protects rat brains against focal ischemia. *Brain Res*. 2009 Jul 28;1282:133-41. [PMID: 19445907]
9. Pugazhenthi S, et al. Regulation of heme oxygenase-1 expression by demethoxy curcuminoids through Nrf2 by a PI3-kinase/Akt-mediated pathway in mouse beta-cells. *Am J Physiol Endocrinol Metab*. 2007 Sep;293(3):E645-55. [PMID: 17535857]
10. Romeo L, et al. The major green tea polyphenol, (-)-epigallocatechin-3-gallate, induces heme oxygenase in rat neurons and acts as an effective neuroprotective agent against oxidative stress. *J Am Coll Nutr*. 2009 Aug;28 Suppl:492S-499S. [PMID: 20234037]
11. Zhang ZM, et al. Modulation of NRF2 and UGT1A expression by epigallocatechin-3-gallate in colon cancer cells and BALB/c mice. *Chin Med J (Engl)*. 2009 Jul 20;122(14):1660-5. [PMID: 19719968]
12. Na HK, et al. (-)-Epigallocatechin gallate induces Nrf2-mediated antioxidant enzyme expression via activation of PI3K and ERK in human mammary epithelial cells. *Arch Biochem Biophys*. 2008 Aug 15;476(2):171-7. [PMID: 18424257]
13. Artali R. Green tea catechins in chemoprevention of cancer: a molecular docking investigation into their interaction with glutathione S-transferase (GST P1-1). *J Enzyme Inhib Med Chem*. 2009 Feb;24(1):287-95. [PMID: 18825537]
14. Hu L, et al. Putative chemopreventive molecules can increase Nrf2-regulated cell defense in some human cancer cell lines, resulting in resistance to common cytotoxic therapies. *Cancer Chemother Pharmacol*. 2010 Aug;66(3):467-74. [PMID: 19940992]
15. Sabinsa. BioPerine® and Curcumin. http://www.bioperine.com/curcumin.html. Accessed October 10, 2010.

Additional references available upon request

EXCLUSIVE • PATENTED

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

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